System Biology and Signal Processing for Biomedical Applications

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My Research Focus

- Filter banks and wavelets (signal processing related)
  - Perfect reconstruction of nonuniform filter banks.
  - Filter banks with block sampling structures.
  - Compressions with applications to scalable JPEG image coding schemes.
  - Denoising with applications to image and biomedical signal processing such as ECG signal and elastogram denoising.
  - Edge detection and edge linking with applications to image processing such as cancer cell image diagnosis and bad potato diagnosis.
  - Signal separations such as audio signal separations for digital audio hearing aids applications and ECG/EMG signal separations, pattern recognitions such as gait recognitions for military applications and fault analysis such as machine fault detections.

My Research Focus

- Optimization (signal processing related)
  - Semi-infinite programming and functional inequality constrained optimizations with applications to filter, filter bank, wavelet kernel, sigma delta modulator and transport system designs.
  - Nonsmooth optimizations with applications to motion estimations as well as filter, filter bank, wavelet kernel and transport system designs.
  - Nonconvex optimizations with applications to spectral allocations for wireless communication networks as well as filter, filter bank, wavelet kernel and transport system designs.
  - Real-time optimizations with applications to filter, filter bank and wavelet kernel designs.

My Research Focus

- Symbolic dynamics, fractal and chaos (control related)
  - Digital filters with two's complement arithmetic and saturation nonlinearity with applications to computer cryptography.
  - Sigma delta modulators with applications to analog-to-digital conversions.
  - Perceptron training algorithms with applications to pattern recognitions.
  - Random early detection mechanisms with applications to internet traffic control.
  - DC/DC converters with applications to industrial and consumer electronic products.
  - Road traffic light signaling with applications to road traffic system control.
  - Nano-particle quantum effect analysis with applications to nano-device fabrications.
  - Rainfall prediction.

My Research Focus

- Control theories (control related)
  - Fuzzy control with applications to time delay feedback systems, sample data control systems and chaos synchronization systems.
  - Optimal switching control with applications to DC/DC converters and transport systems.
  - Impulsive control with applications to sigma delta modulators.
  - Chaos control with applications to TCPIP networks, HIV model systems and avian influenza model systems.

Outline

- Introduction
- HIV Control
- Avian Influenza Control
- Cough Analysis
- Elastogram Denoising
- Data Mining for Cancer Cell Diagnosis
- Biometrics and Digital Forensics
- References
- Questions and Answers

Introduction

- What is System Biology?
  - Systems biology is the study of the interactions among the components of *biological systems*, and how these interactions give rise to the function and behaviour of that system.

Introduction

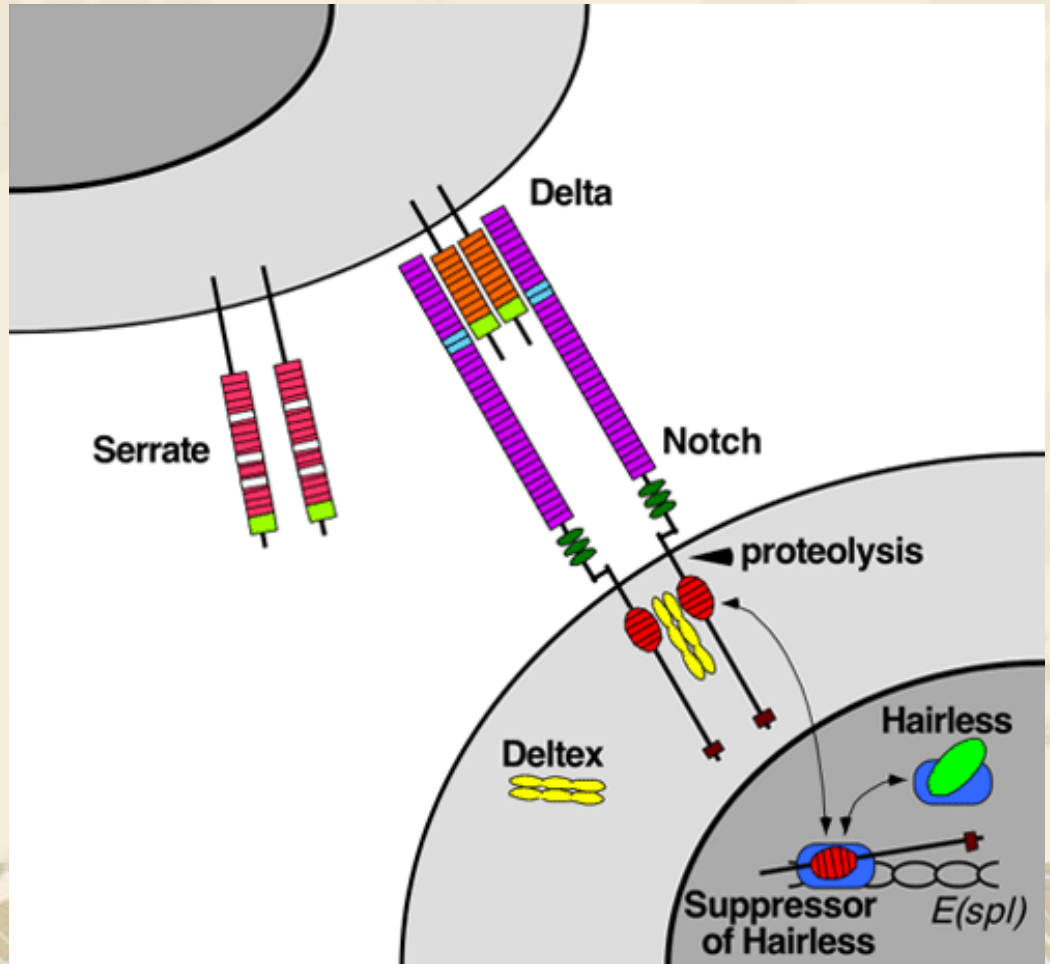
- Cell Signalling
  - Cells are communicated and connected each others.
  - Examples
    - signal exchange between early embryo cells and cells of the uterus
    - signal exchange between bacteria and human epithelial and immune system cells in the human gastrointestinal tract.
  - Type of signalling
    - Juxtacrine signalling (direct contact)
    - Paracrine signalling (over short distances)
    - Endocrine signalling (over large distances)

Introduction

- Cell Signalling
  - Direct contact
    - Cells form gap functions that connect their cytoplasm to the cytoplasm of adjacent cells.
    - Example
      - Gap functions between adjacent cells of cardiac muscle allow propagation of action potential from the cardiac pacemaker region to adjacent regions of the heart so as to spread and coordinately cause contraction of the heart.

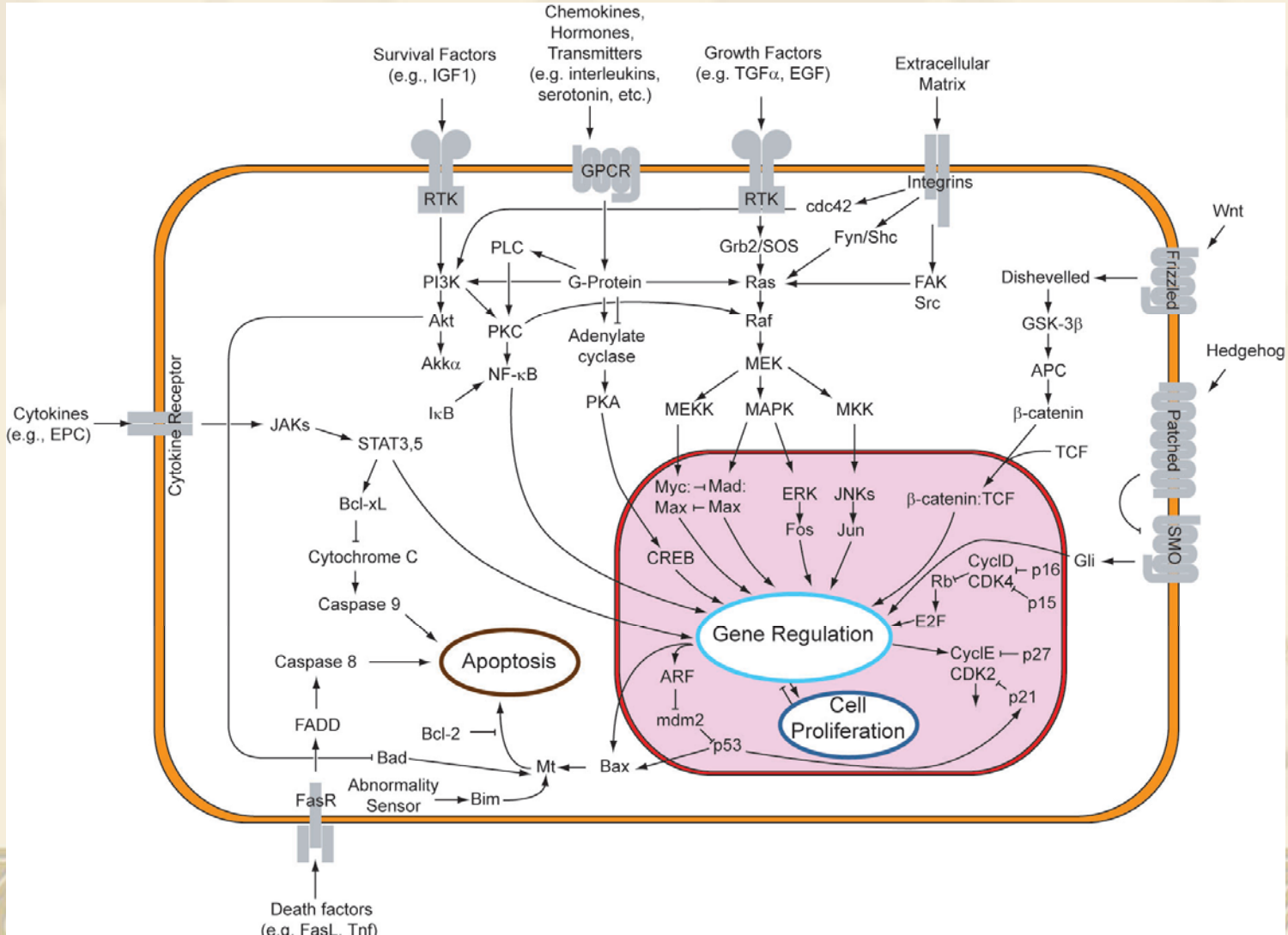
Introduction

- Cell Signalling
  - Notch signalling



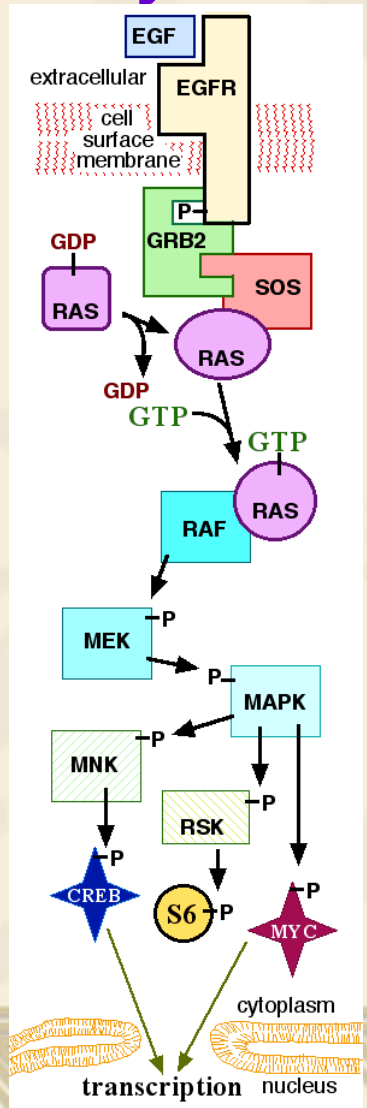
Introduction

- Signalling Pathways



Introduction

- Signalling Pathways

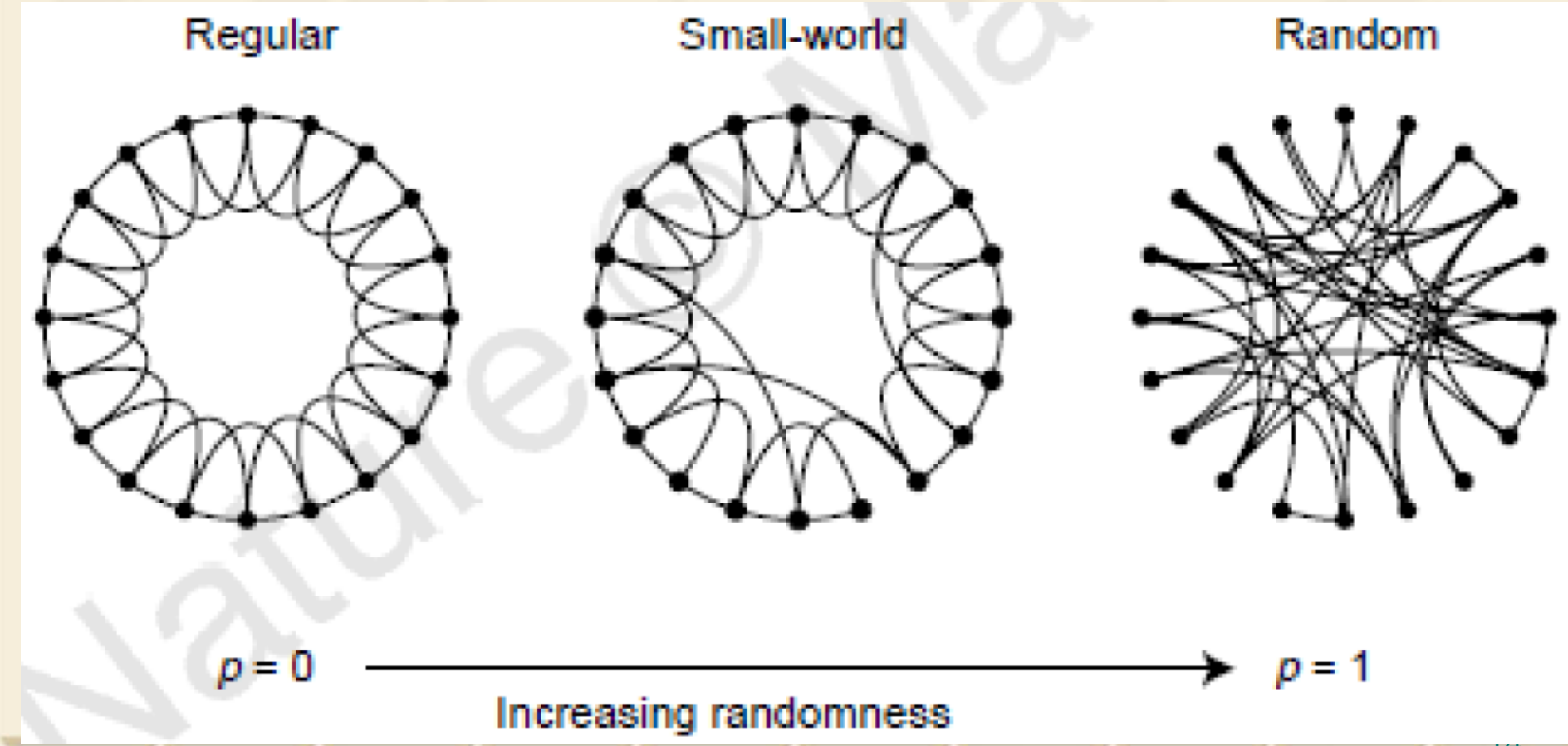


Introduction

- Complex Network Aspect
  - Complex networks are networks with nontrivial topological features, such as a heavy tail in the degree distribution, a high clustering coefficient, assortativity or disassortativity among vertices.
  - Types of complex networks
    - Scale free networks
    - Small world networks
    - Regular networks
    - Random networks

Introduction

- Complex Network Aspect
  - Types of complex networks



Introduction

- Complex Network Aspect
  - There are billions of cells communicated each others.
  - The network of cells is actually a complex network.

Introduction

- Complex Behaviours of Cells
  - The dynamics characterizing the behaviours of cells are nonlinear.
  - When virus attacks the cells or the cells are excited to another states, the cell could exhibit very complex behaviours, such as chaotic behaviours.

HIV Control

- System Model

$$\frac{d}{dt}x(t) = a(x_0 - x(t)) - bx(t)z(t)$$

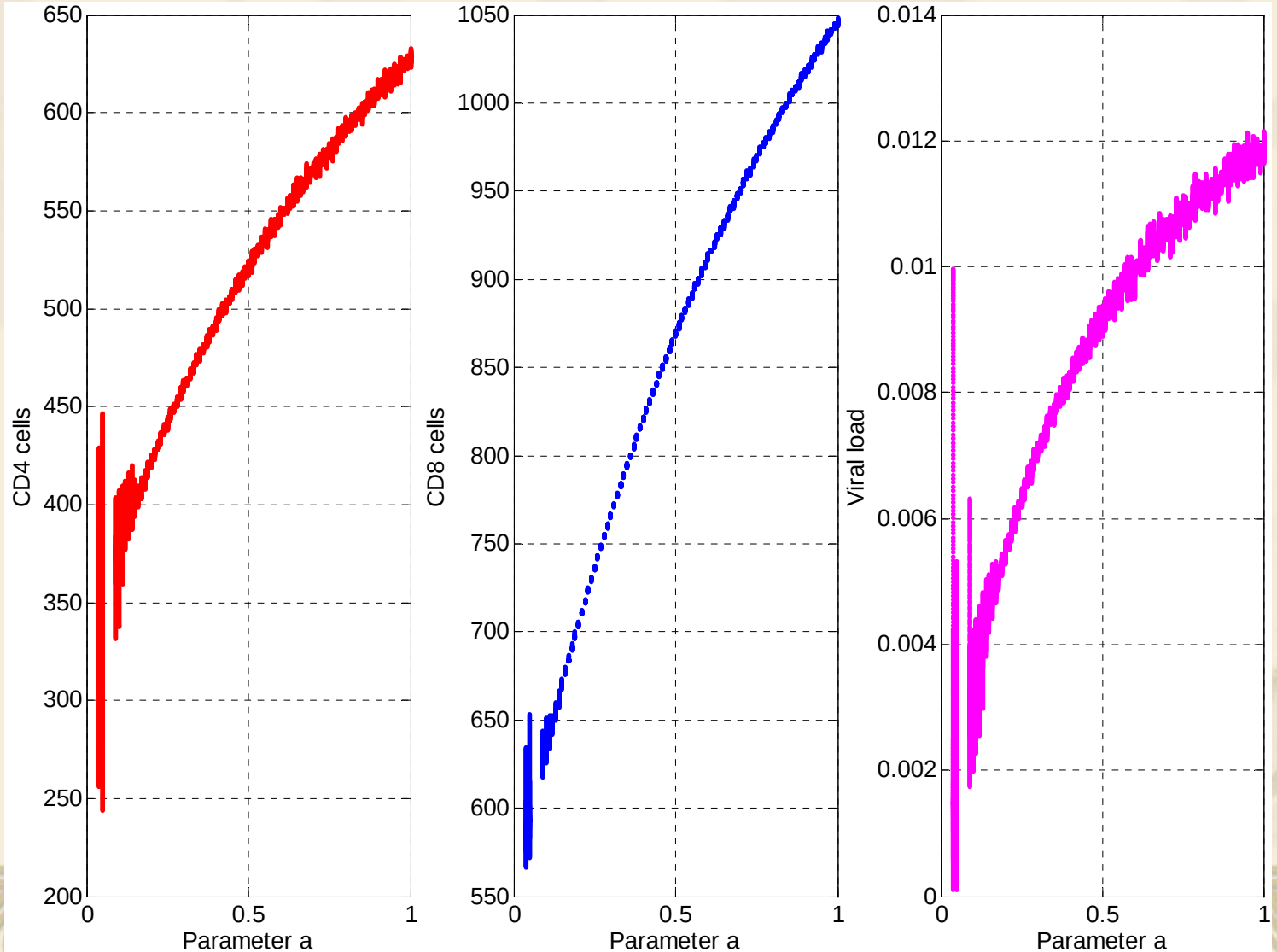
$$\frac{d}{dt}y(t) = c(y_0 - y(t)) + dy(t)z(t)$$

$$\frac{d}{dt}z(t) = z(t)(ex(t) - fy(t))$$

$x(t)$, $y(t)$ and $z(t)$ are the concentrations of the CD4 lymphocyte population, the CD8 lymphocyte population and the HIV-1 viral load, respectively. x_0 and y_0 are the normal unperturbed concentrations of the CD4 and CD8 lymphocyte population, respectively.

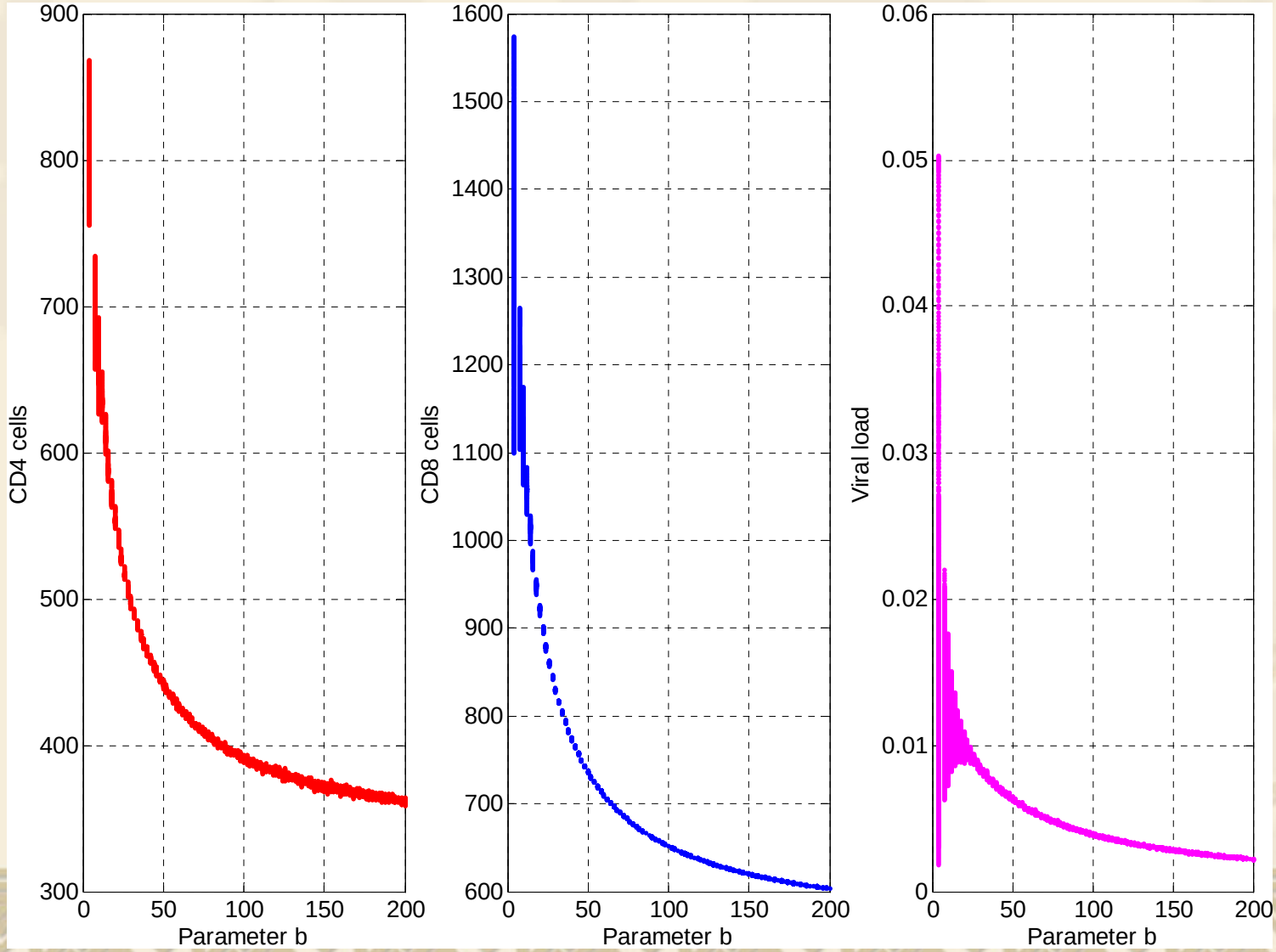
HIV Control

- Bifurcation Behaviours



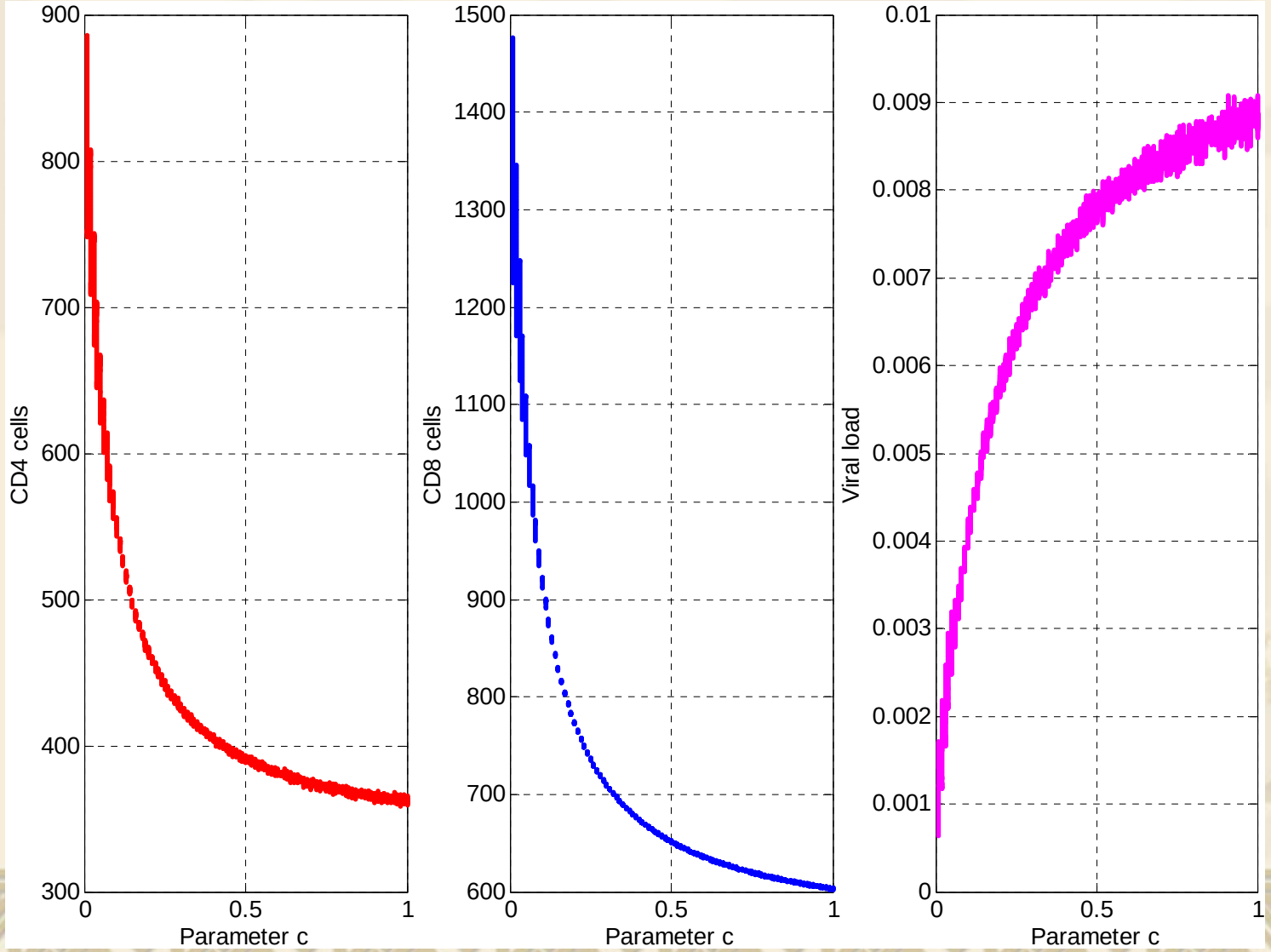
HIV Control

- Bifurcation Behaviours



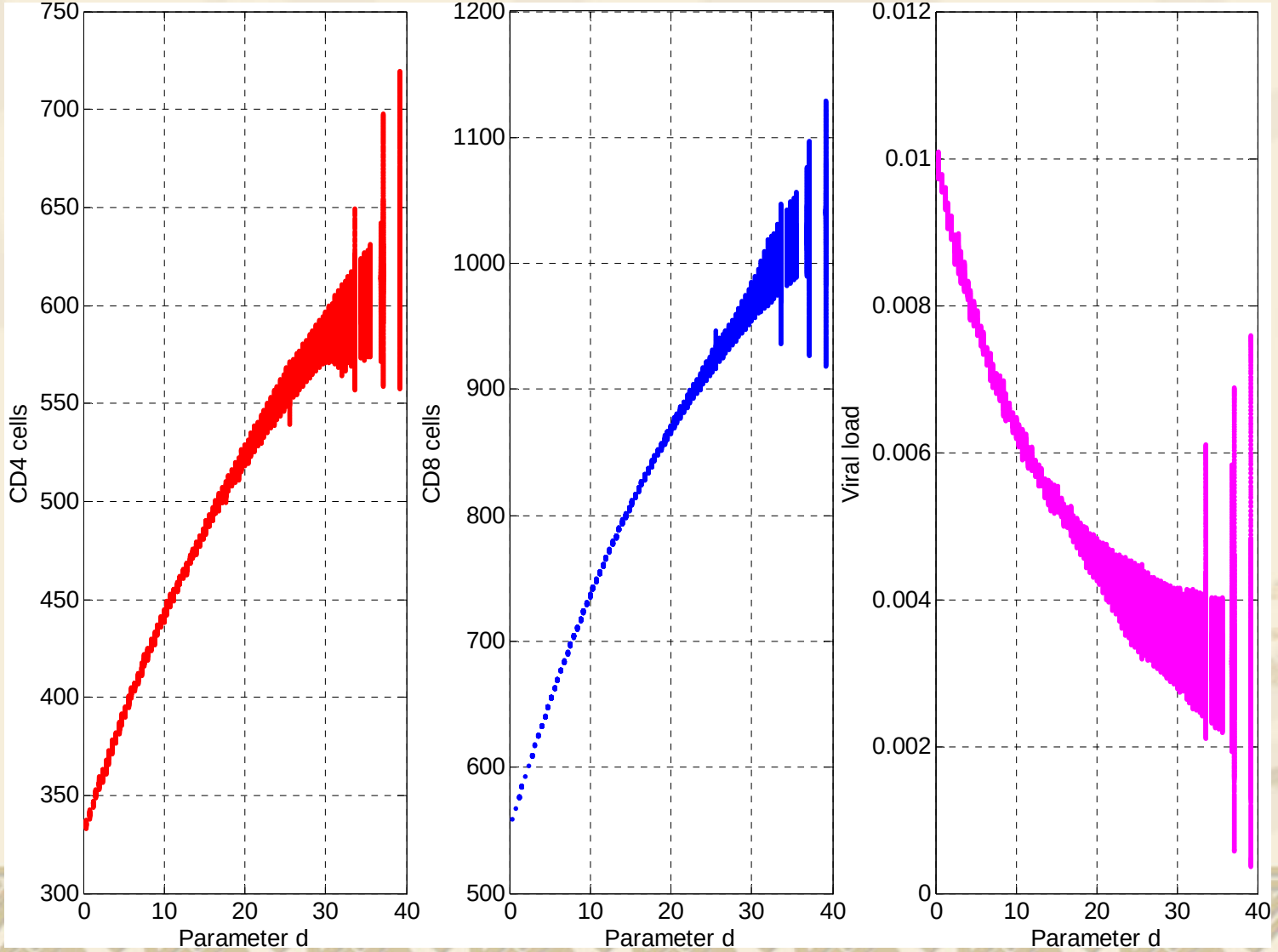
HIV Control

- Bifurcation Behaviours



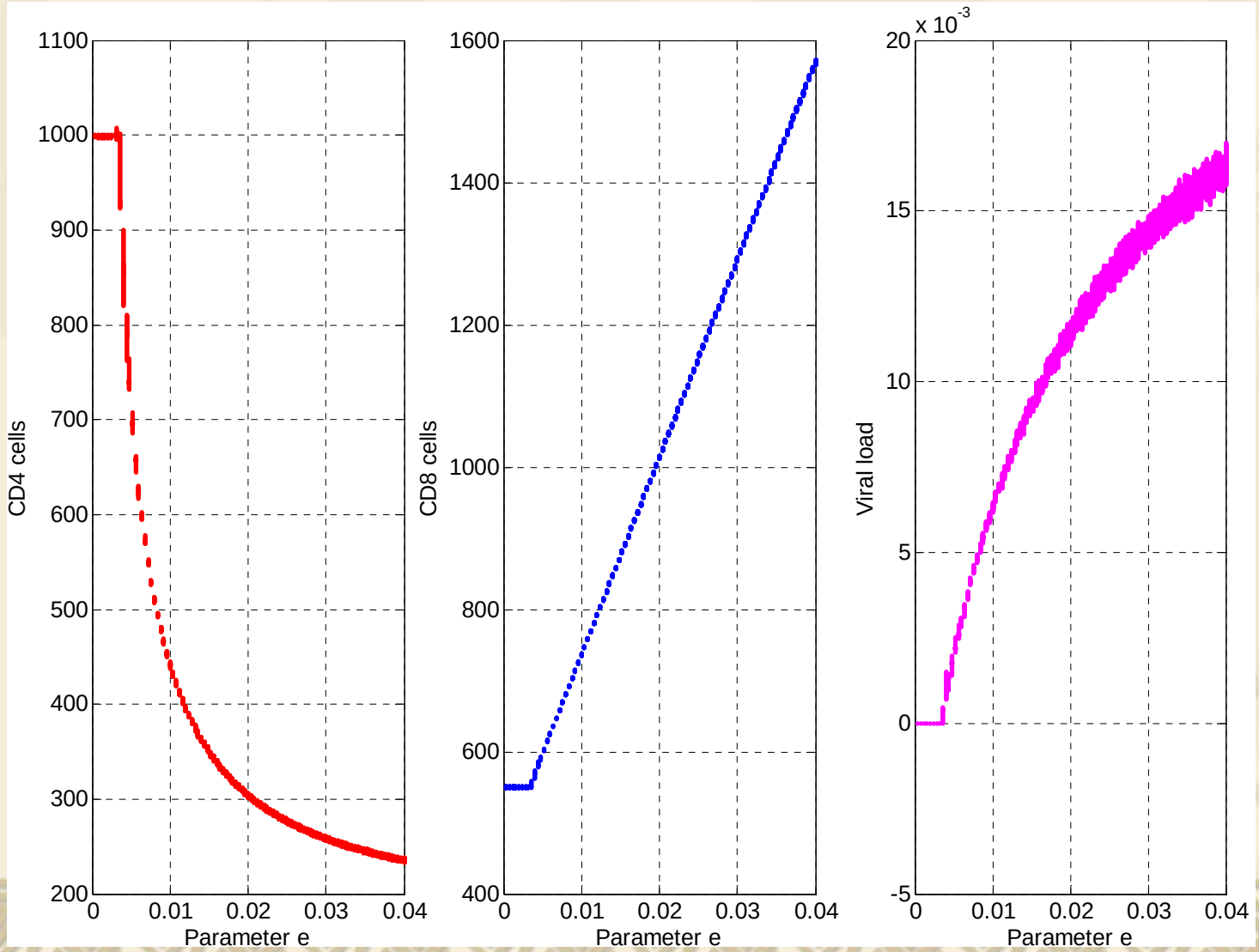
HIV Control

- Bifurcation Behaviours



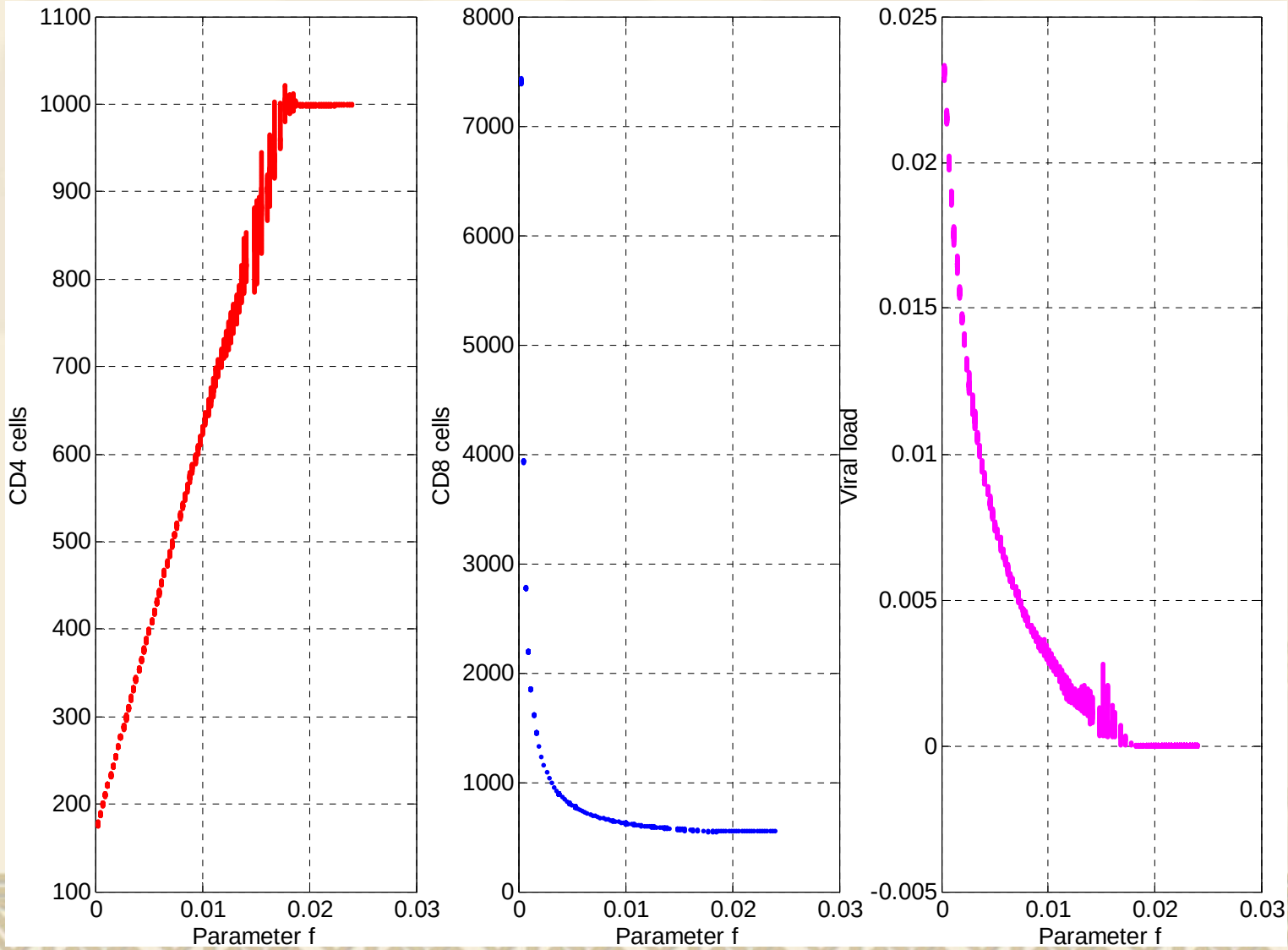
HIV Control

- Bifurcation Behaviours



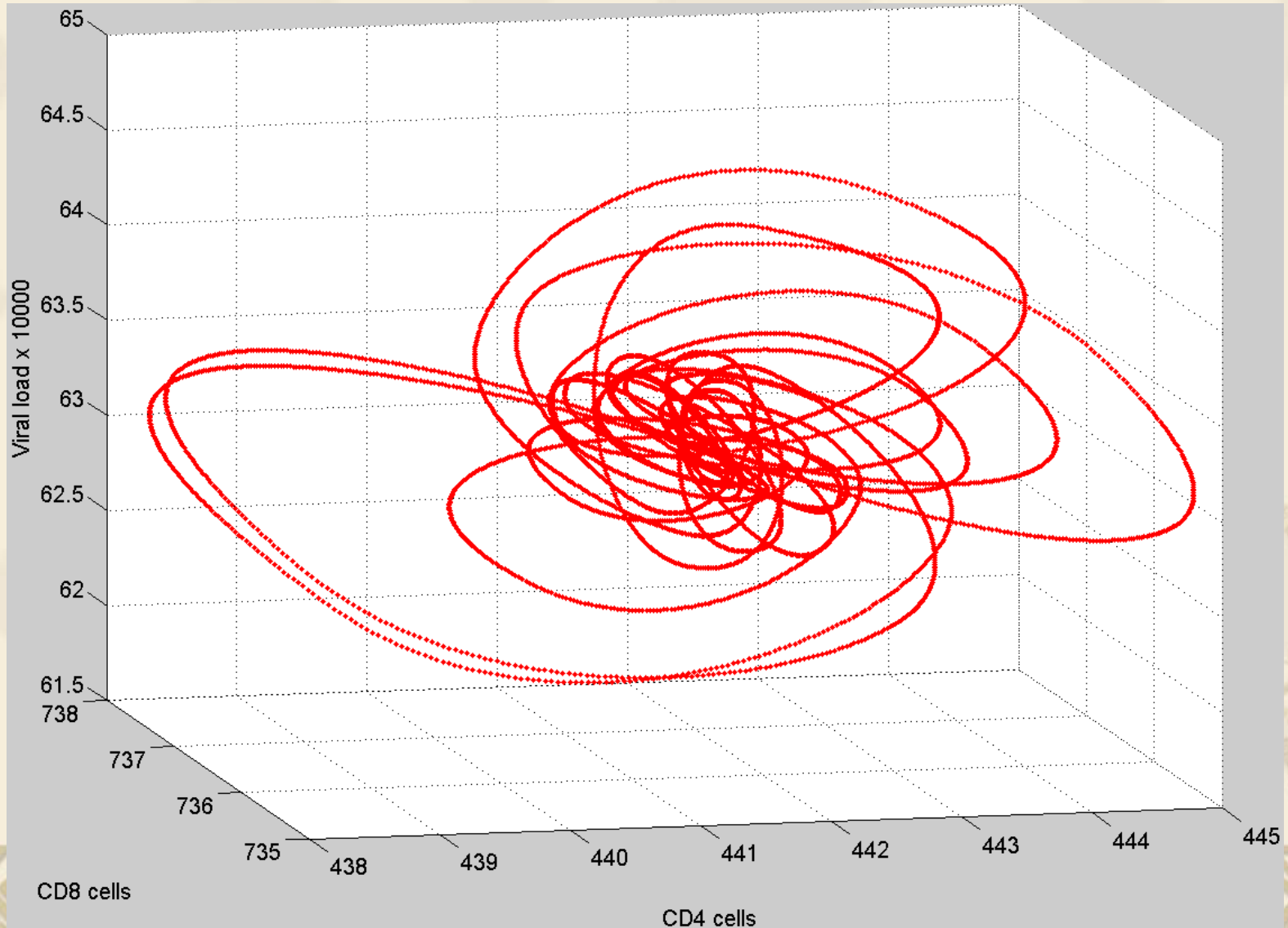
HIV Control

- Bifurcation Behaviours



HIV Control

- Chaotic Behaviours



HIV Control

- Control Aspect
  - There are about 20 medications approved by Food and Drug Administration (FDA) of the US government and these medications are used for suppressing HIV.
  - Strategy for applying drugs is actually a control problem.

HIV Control

- Control Model

$$\frac{d}{dt}x(t) = a(x_0 - x(t)) - bx(t)z(t)$$

$$\frac{d}{dt}y(t) = c(y_0 - y(t)) + dy(t)z(t)$$

$$\frac{d}{dt}z(t) = z(t)(ex(t) - fy(t)) - U(t)$$

$U(t)$ is the dose of medications.

HIV Control

- Challenges
  - The system is nonlinear. Linear control methods such as proportional control (The higher the viral load corresponds to the higher the dose of medications.) do not apply.
  - The linearized system is uncontrollable at the equilibrium point. Hence, it will lose control near the equilibrium point.
  - Practical considerations, such as positivity requirements (The concentration of CD4 cells, CD8 cells, viral load and medications must be positive.) and the side effects of the chemotherapy (The dose cannot be higher than certain levels.) should be exploited in the control.

HIV Control

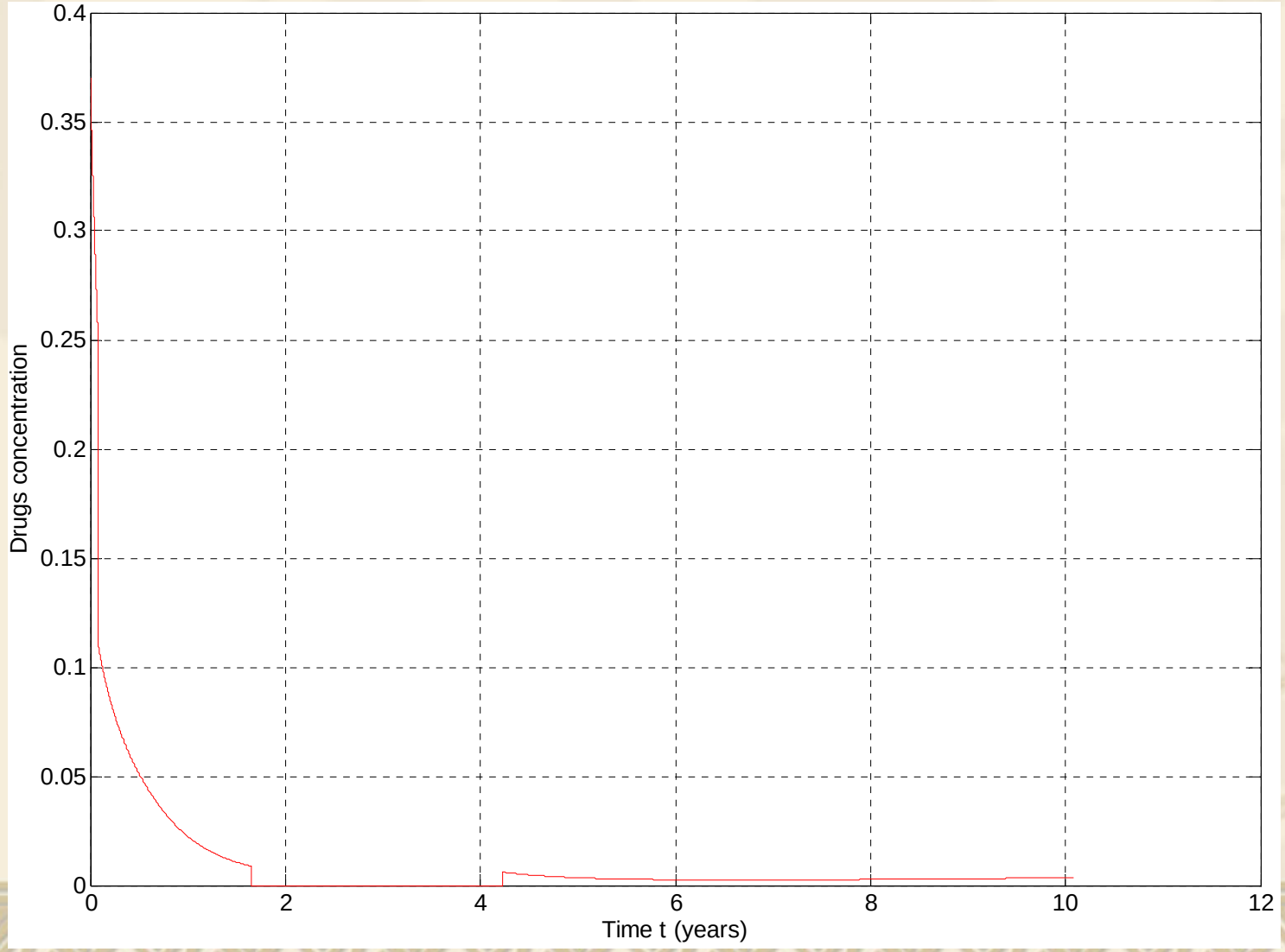
- Existing Control
  - Proportional control is used.
  - Control cannot be stopped. That means, if the patients are suffered from HIV, the patients have to take the drugs and suffer the side effects of the chemotherapy until they die. This is a bad news to patients.

HIV Control

- Proposed Control
  - Stop applying dose for certain period of time.
  - Guarantee the following:
    - Positivity requirements are satisfied.
    - Dose applied is below a certain threshold value and this threshold value can be assigned according to different patients. Hence, the maximum side effects that the patients have to be suffered is guaranteed and tailor made according to the patients.
    - The viral load is monotonic decreasing.

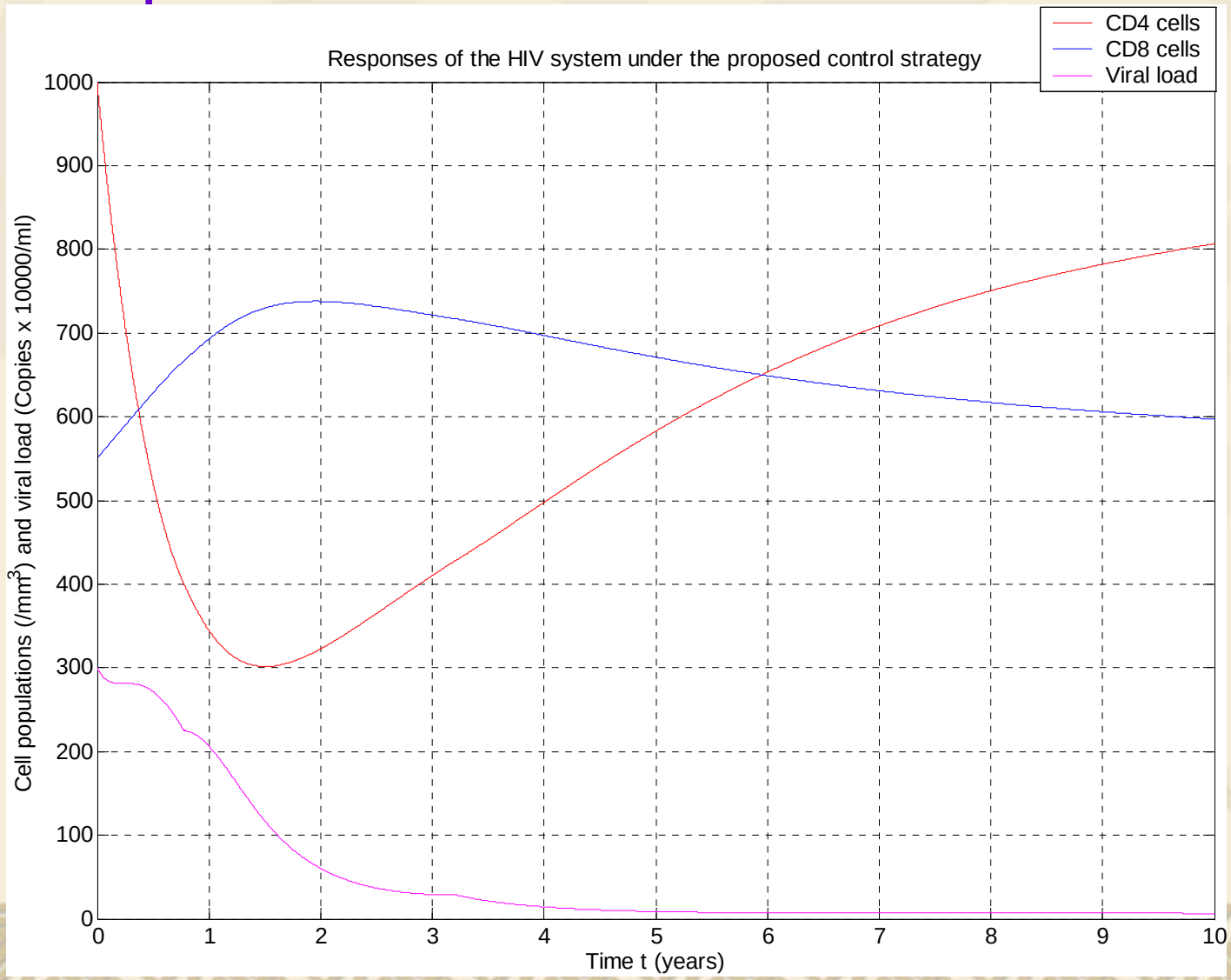
HIV Control

- Computer Numerical Simulation Results



HIV Control

- Computer Numerical Simulation Results



Avian Influenza Control

- System Model

$$\frac{dX(t)}{dt} = c - bX(t) - \omega X(t)Y(t)$$

$$\frac{dY(t)}{dt} = \omega X(t)Y(t) - (b+m)Y(t)$$

$$\frac{dS(t)}{dt} = \lambda - \mu S(t) - \beta_1 Y(t)S(t) - \beta_2 H(t)S(t)$$

$$\frac{dB(t)}{dt} = \beta_1 Y(t)S(t) - (\mu + d_1)B(t)$$

$$\frac{dH(t)}{dt} = \beta_2 H(t)S(t) - (\mu + d_2)H(t)$$

Avian Influenza Control

- System Model

  $X(t), Y(t), S(t), B(t)$ and $H(t)$ are the populations of susceptible birds, birds infected with wild avian influenza, susceptible humans, humans infected with wild avian influenza and humans infected with mutant avian influenza, respectively.

Avian Influenza Control

- Types of Control
  - Elimination control
    - Apply to the birds implemented by a killing action.
  - Quarantine control
    - Apply to the humans implemented by a vaccine injection.

Avian Influenza Control

- Control Model

$$\frac{dX(t)}{dt} = c - bX(t) - (1-u_1(t))\omega X(t)Y(t)$$

$$\frac{dY(t)}{dt} = (1-u_1(t))\omega X(t)Y(t) - (b+m)Y(t)$$

$$\frac{dS(t)}{dt} = \lambda - \mu S(t) - \beta_1 Y(t)S(t) - (1-u_2(t))\beta_2 H(t)S(t)$$

$$\frac{dB(t)}{dt} = \beta_1 Y(t)S(t) - (\mu + d_1)B(t)$$

$$\frac{dH(t)}{dt} = (1-u_2(t))\beta_2 H(t)S(t) - (\mu + d_2)H(t)$$

$u_1(t)$ and $u_2(t)$ are the elimination control force and the quarantine control force, respectively.

Avian Influenza Control

- Challenge
  - The control has to satisfy the positivity requirements.
  - Both the control forces have to be bounded by one.
  - The system is also nonlinear. Linear control methods do not apply.
  - The control forces are not additive to the system state variables. Instead, they are multiplicative. Hence, the system exhibits very complex behaviours.

Avian Influenza Control

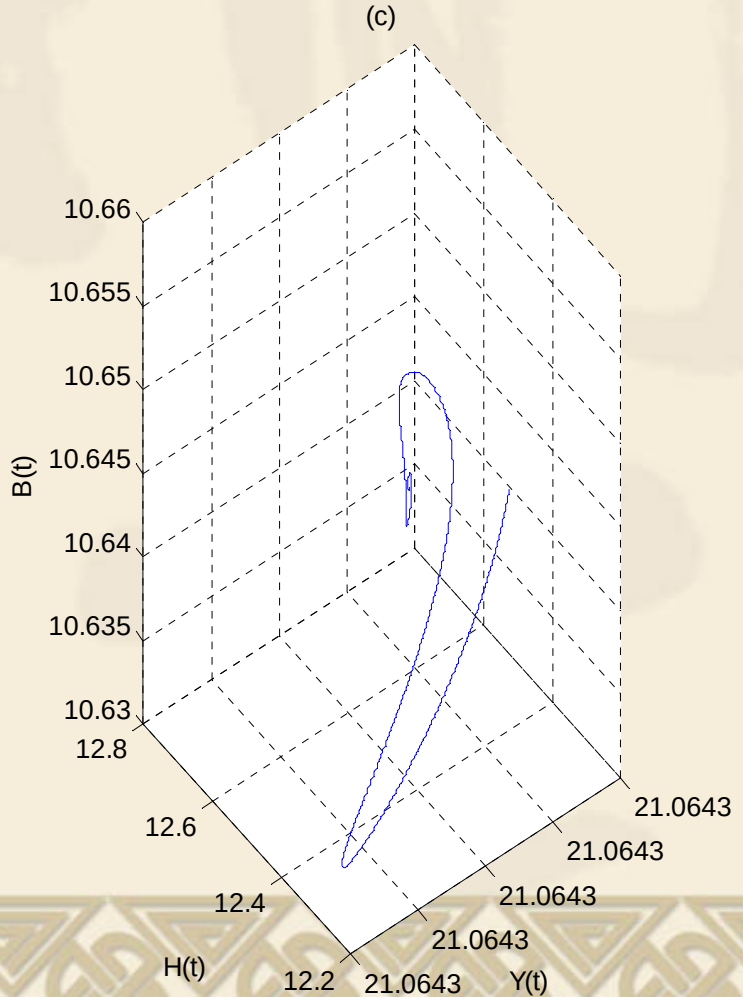
- Existing Control
  - If there is a bird infected with wild avian influenza, then a full elimination control force is applied.
  - If there is a human infected with wild avian influenza or a human infected with mutant avian influenza, then a full quarantine control force is applied.

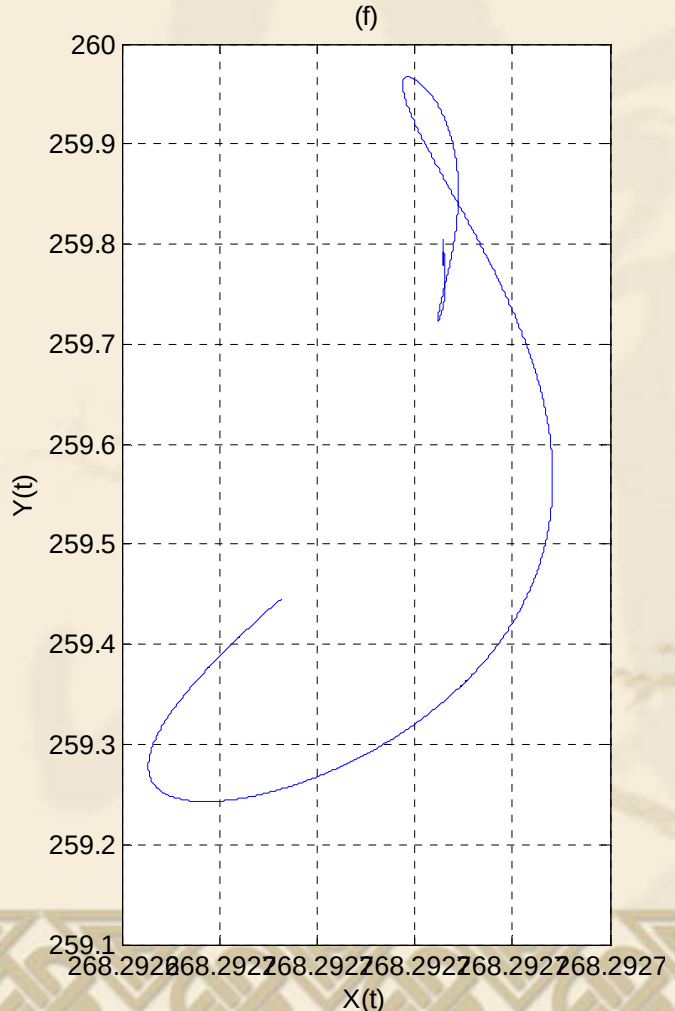
Avian Influenza Control

- Proposed Control
  - Stop applying control for certain period of time.
  - Guarantee the following:
    - Positivity requirements are satisfied.
    - The applied control forces are bounded by one.
    - The system converges to the equilibrium point.

Avian Influenza Control

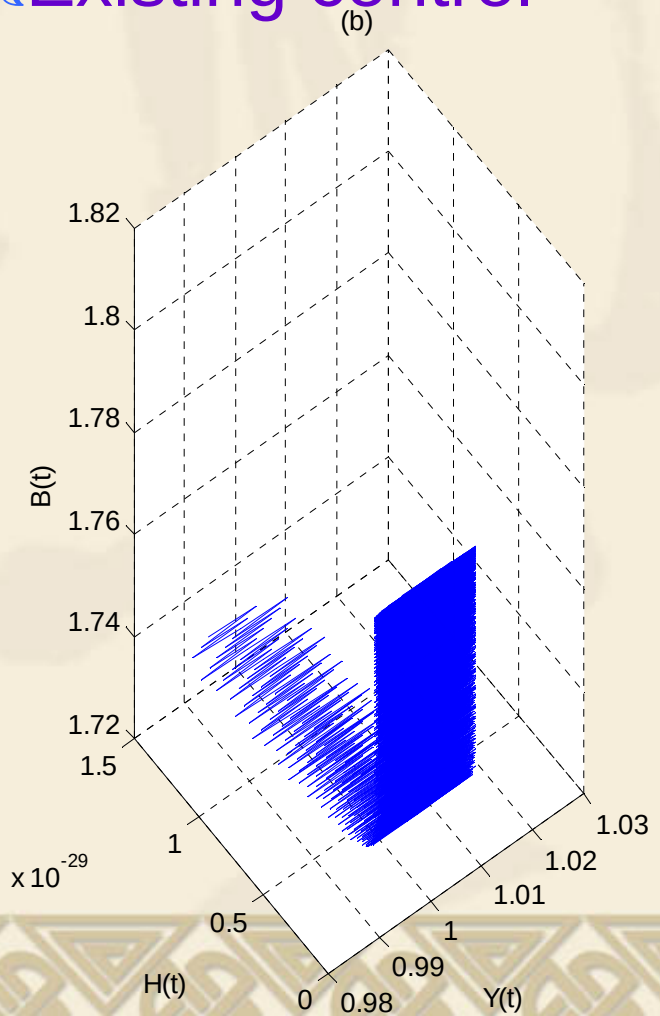
- Computer Numerical Simulation Results
  - Without control

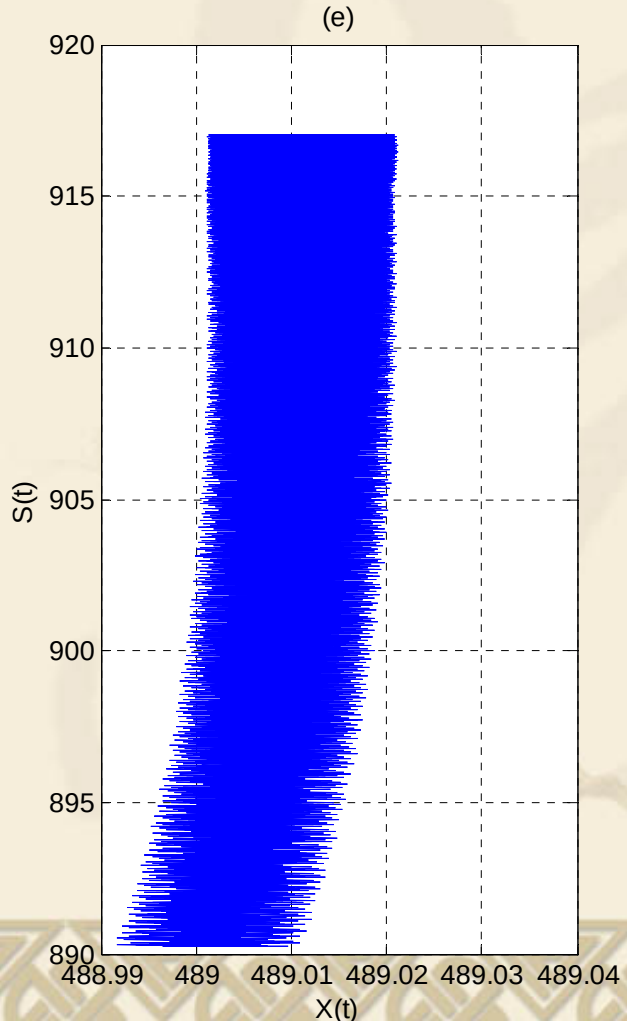




Avian Influenza Control

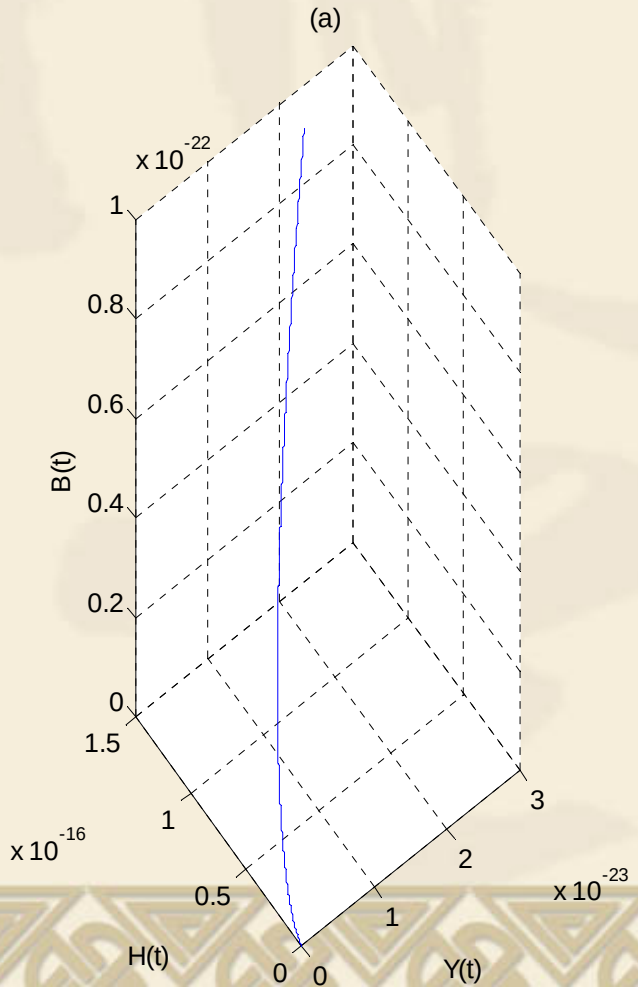
- Computer Numerical Simulation Results
  - Existing control

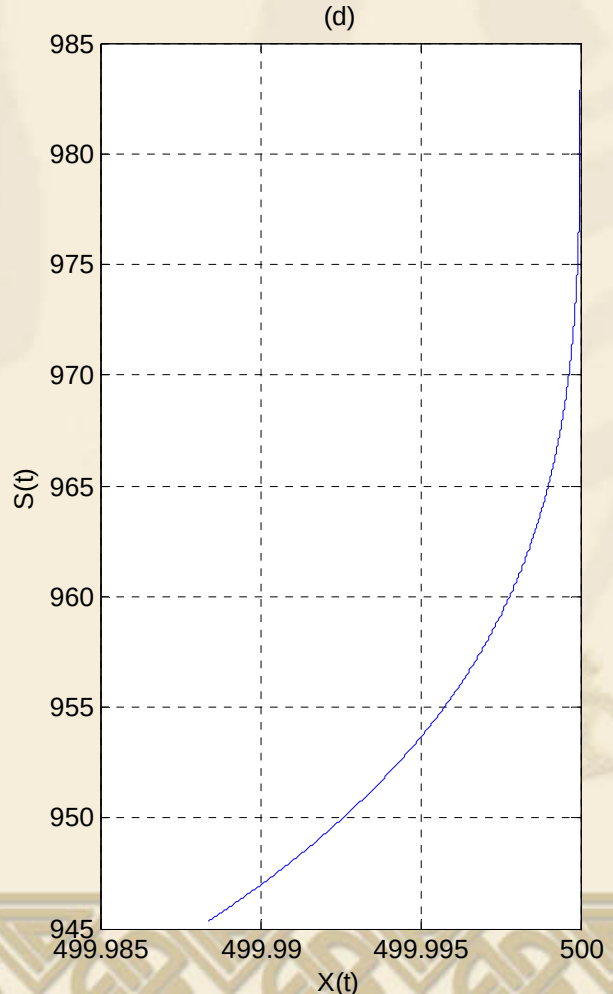




Avian Influenza Control

- Computer Numerical Simulation Results
  - Our proposed control





Cough Analysis

- Background
  - Diagnosis of complicated cough problems are based on physiological measurements.
  - The equipments for obtaining these physiological measurements are very expensive.
  - Only several hospitals in UK have these equipments.
  - All GPs refer their patients to these hospitals. As a result, these hospitals are severely loaded.

Cough Analysis

- Objective
  - Develop a low cost and portable device based on cough sounds so that GPs could perform the diagnosis by themselves.

Cough Analysis

- Challenges
  - Different patients have different cough sounds.
  - Even though for the same patient, the cough sounds at different time instants are different.
  - The relationship between the cough sounds and these physiological measurements are unknown.
  - The implementation of the algorithm is very low. It is less than £10.
  - The diagnosis has to be implemented in real-time.

Cough Analysis

- Ideas
  - The nature of cough sounds and audio sounds without vowels is very similar.
  - Techniques in audio sound recognition is applied for the recognition of cough sounds.

Elastogram Denoising

- What is Elastogram?
  - Elastogram is a type of non-invasive images in which the Young's modulus distribution across an object is captured.

Elastogram Denoising

- Application of Elastogram
  - A tumour or suspicious cancerous tissues are normally 5 to 28 times stiffer than normal soft tissues.
  - When a mechanical compression or a vibration is applied, the tumour deforms less than surrounding tissues.
  - This implies that the strain in the tumour is less than that of the surrounding tissues.
  - By capturing the image showing the Young's modulus distribution across the cells, a tumour can be detected and classified.
  - Elastograms can be used for the detection and the classification of tumours.

Elastogram Denoising

- Why Noise Found in Elastogram?
  - Ultrasonic imaging is the most common medical imaging for producing elastograms because the cost is low, the time required for producing images is short and the device is portable.
  - Ultrasonic images are usually very noisy.

Elastogram Denoising

- Existing Denoising Technique
  - Lowpass filtering technique, in which the values of the pixels of the denoising elasrogram are the weighted sum of the values of their neighbourhood pixels.
  - However, lowpass filtering will damage the edge.

Elastogram Denoising

- Time Frequency Mask Technique
  - Filtering the elastogram.
  - Applying a window to extract the region of the cell.
  - Implementation
    - Filtering is equivalent to applying a mask in the frequency domain.
    - Converting a signal from its time domain to its frequency domain is equivalent to multiplying the vector of the signal by the discrete Fourier transform matrix.
    - Hence, filtering is equivalent to **FUy**, where **U** is the discrete Fourier transform matrix, **F** is a diagonal matrix with its diagonal elements being the mask coefficients, and **y** is the vector of the signal.

Elastogram Denoising

- Time Frequency Mask Technique
  - Implementation
    - Windowing is equivalent to applying a mask in the time domain.
    - Converting a signal from its frequency domain to its time domain is equivalent to multiplying the vector of the signal by the inverse discrete Fourier transform matrix.
    - Hence, windowing is equivalent to $\mathbf{WU}^{H}\mathbf{z}$, where the superscript “H” denotes the Hermitian operator, **W** is a diagonal matrix with its diagonal elements being the mask coefficients, and **z** is the vector of the signal.

Elastogram Denoising

- Generalization of Time Frequency Mask Technique
  - Discrete Fourier transform matrix is a particular Hermitian matrix, that is $\mathbf{U}^H\mathbf{U}=\mathbf{I}$.
  - Instead of transforming the signal to the frequency domain and applying a mask on its frequency components, then inverse transforming the signal back to the time domain and applying another mask on its time domain, better result is expected if a better Hermitian transform is applied.

Elastogram Denoising

- Generalization of Time Frequency Mask Technique
  - Problem formulation

$$\min_{(\mathbf{U},\mathbf{f},\mathbf{w})} J(\mathbf{U},\mathbf{f},\mathbf{w}) \equiv \sum_{i=0}^{M-1} \left\| \mathbf{W}\mathbf{U}^H \mathbf{F}\mathbf{U}\mathbf{y}_i - \mathbf{x}_i \right\|^2$$

subject to $\mathbf{U}\mathbf{U}^H = \mathbf{U}^H\mathbf{U} = \mathbf{I}_{N\times N}$

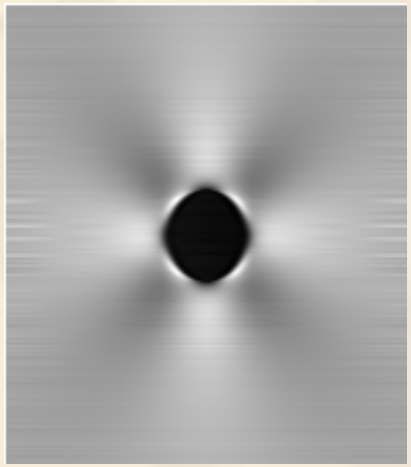
where M is the total number of training elastogram, $\mathbf{y}_i$ and $\mathbf{x}_i$ are the noisy and the desirable clean elastogram, respectively.

Elastogram Denoising

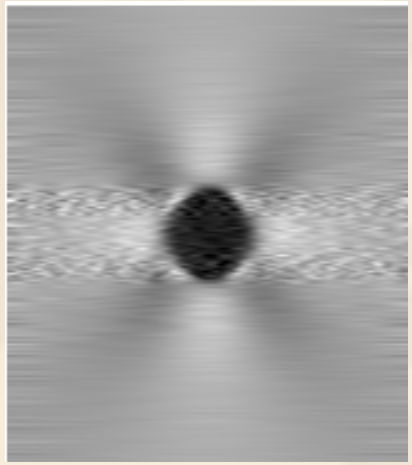
- Generalization of Time Frequency Mask Technique
  - Challenge
    - To optimization these two diagonal matrices **W** and **F** and a complex valued matrix **U** simultaneously, the optimization problem is highly nonlinear and nonconvex.
    - The Herimtian constraint is quadratic. It is challenge to guarantee the satisfaction of a quadratic constraint.
    - Analytical solution of the optimization problem is necessary because it consists of a large training set of elastograms.

Elastogram Denoising

- Computer Numerical Simulation Results

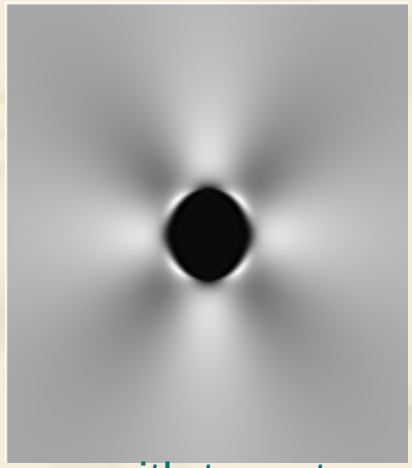


Ideal elastogram



Elastogram with single stage filtering

Corrupted elastogram



Elastogram with two stage filtering

Data Mining for Cancer Cell Diagnosis

- Useful Information for Cancer Cell Diagnosis
  - Average size of cancer cells
  - Shape of cancer cells
  - Colour of cancer cells
  - Number of cancer cells

Data Mining for Cancer Cell Diagnosis

- Challenges
  - Edge of cancer cells are not clearly defined. Hence, the size and the shape of cancer cells are not easy to be quantified.

Data Mining for Cancer Cell Diagnosis

- Existing Approaches
  - There are two types of edge detection scheme. The first type of edge detection scheme is based on a first order derivative type bandpass filtering and a thresholding scheme, while the second type of edge detection scheme is based on a second order derivative type bandpass filtering and a zero crossing searching scheme.

Data Mining for Cancer Cell Diagnosis

- Existing Approaches
  - The edge filters pick up noise in their corresponding passbands. Hence, the filtered cancer cell images are very noisy.
  - The obtained edges are discontinuous.

Data Mining for Cancer Cell Diagnosis

- Our Proposed Approach
  - Fuzzy approach
    - Classical set theory tells us that an element is either in a set or not, but fuzzy set theory tells us that an element is in a set associated with a membership function with the membership functional value between zero and one.
    - When the membership functional value is equal to zero, this reduces to the classical case that the element is not in the set. Similarly, when the membership functional value is equal to one, this reduces to the classical case that the element is in the set.

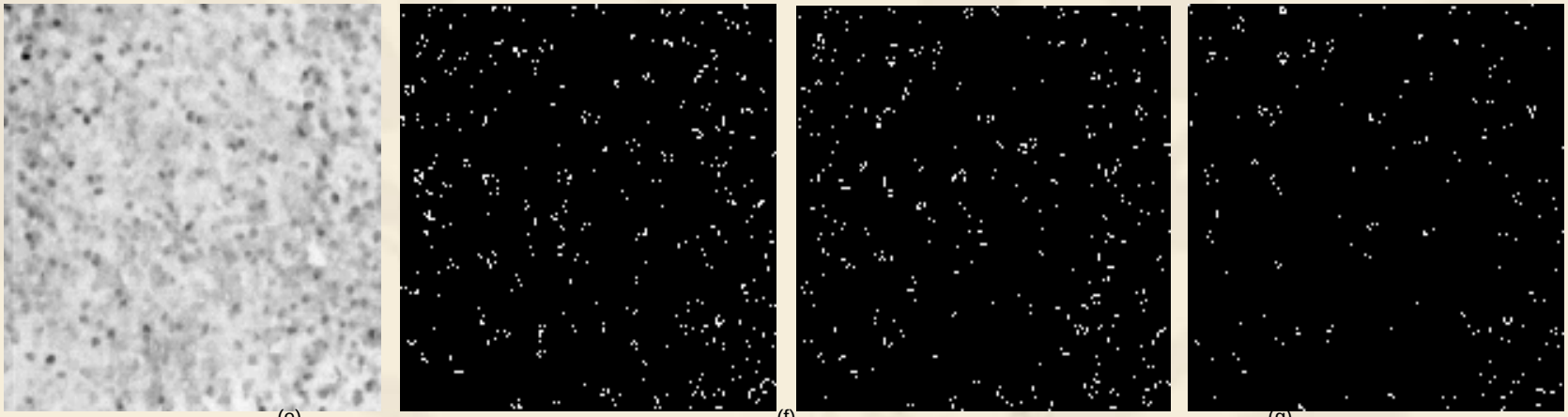
Data Mining for Cancer Cell Diagnosis

- Our Proposed Approach
  - Fuzzy approach
    - Classical logic is binary and characterized by a truth table. Fuzzy logic characterizes the logic value of the input and output pair by a fuzzy membership function.
    - The outputs of different edge filters are normalized and used as the fuzzy membership functions of individual filters.
    - Fuzzy rules are defined on these fuzzy membership functions.
    - The defuzzification is based on a thresholding approach.

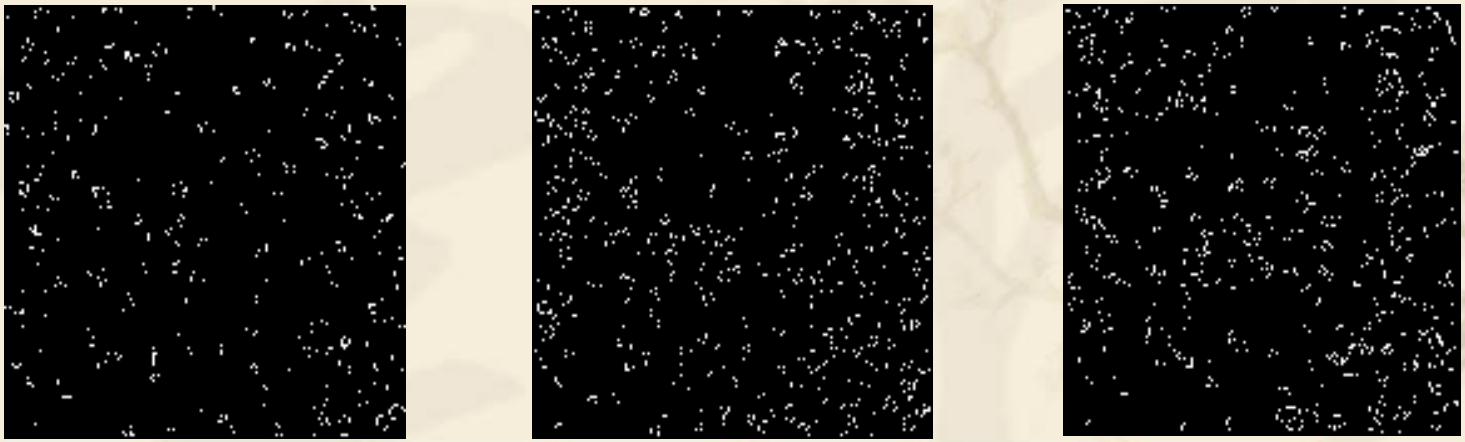
Data Mining for Cancer Cell Diagnosis

- Computer Numerical Simulation Results

(a) (b) (c) (d)



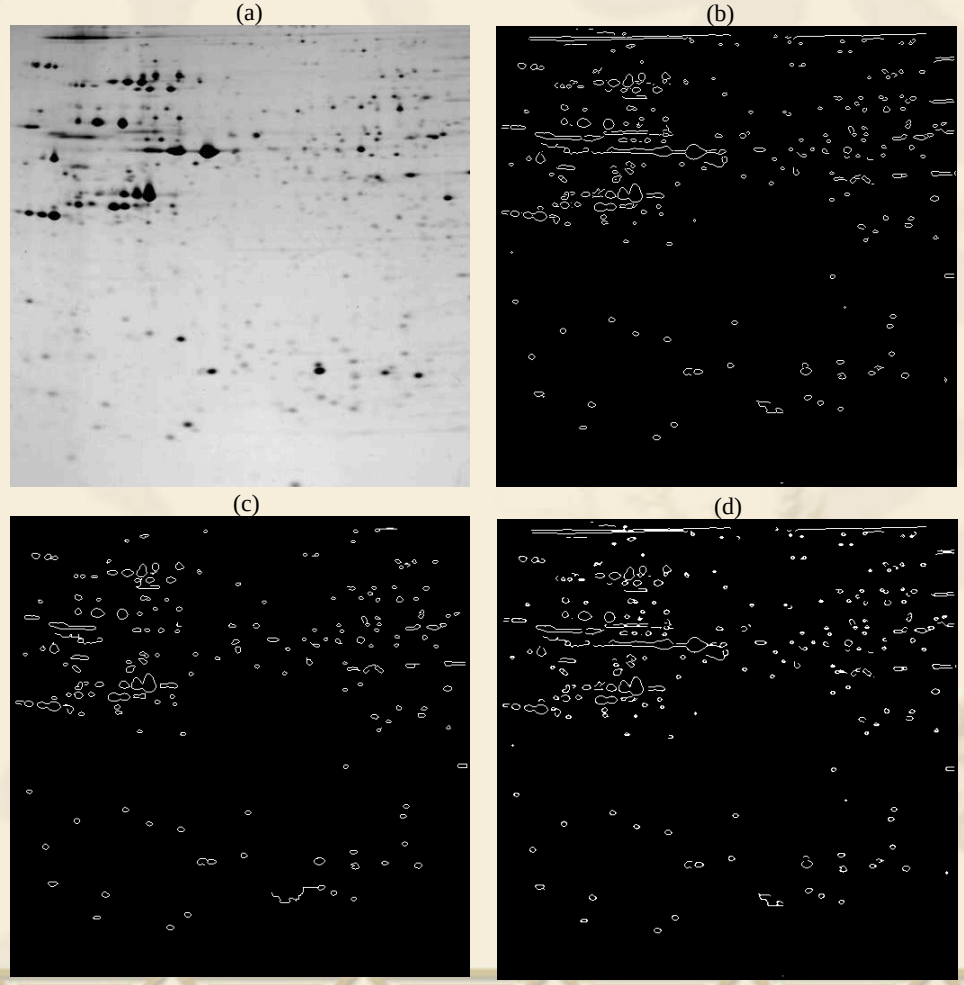
(e) (f) (g)



Results of different edge detectors on the image “Cancer”. (a) original image (b) output of Sobel filter (c) output of Prewitt filter (d) output of Roberts filter (e) output of Isotropic filter (f) output of Canny filter (g) output of our proposed fuzzy switch

Data Mining for Cancer Cell Diagnosis

- Computer Numerical Simulation Results



(a) Cancer image of patient D (b) output at the fuzzy edge detector (c) output at the fuzzy edge linking module (d) output of edge linking module using existing approaches.

Biometrics and Digital Forensics

- What is Digital Forensics?
  - A branch of forensic science pertaining to legal evidence found in computers and digital storage media.

Biometrics and Digital Forensics

- Interests in Digital Forensics
  - Device identification
  - Device linking
  - Recovery of processing history
  - Detection of digital forgeries

Biometrics and Digital Forensics

- My Research Focus
  - Identify the corresponding mobile handsets based on images and video sequences downloaded from facebook or internet.

Biometrics and Digital Forensics

- Assumption
  - Images and video sequences downloaded from facebook or internet are taken from mobile handsets.

Biometrics and Digital Forensics

- Working Principles
  - Each mobile handset has its own noise profile.
  - By computing the correlation coefficient between the noise profile of two different sets of mobile handsets, two probability density functions are obtained.
  - Recognition and classification can be performed.

Biometrics and Digital Forensics

- Existing Results
  - Existing results focus on the recognition and classification based on image.
  - No result can be found based on video sequences.

Biometrics and Digital Forensics

- Open Problems in Digital Forensics
  - The effects of different video frames (I frames, B frames and P frames) on the probability density functions are unknown.
  - The effects of different video contents (fast video motion sequences, slow video motion sequences, flat field motion sequences and complete black video motion sequences) on the probability density functions are unknown.
  - The effects of different video formats (avi, 3gpp and mpeg) on the probability density functions are unknown.
  - The effects of different image and video signal processing techniques (resizing and clopping) on the probability density functions are unknown.

Biometrics and Digital Forensics

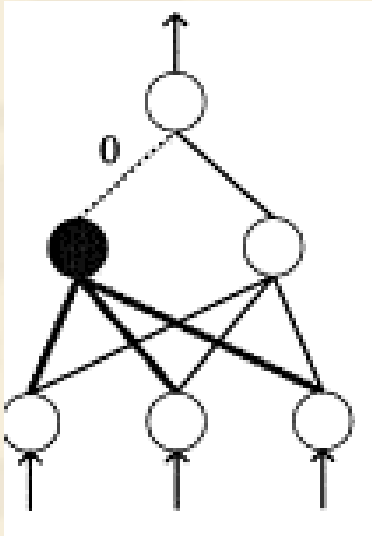
- Open Problems in Digital Forensics
  - The effects of different colour planes (red, green and blue) on the probability density functions are unknown.
  - The thresholds on the probability density functions for classifying different types of mobile handsets are unknown.
  - Whether new techniques, such as using multi-layer perceptrons, could improve the classification rate is unknown.

Biometrics and Digital Forensics

- Technique Involved
  - Optimization
  - Statistical signal processing
  - Neural networks
  - Pattern recognition
  - Image and video signal processing

Biometrics and Digital Forensics

- Optimization for Digital Forensics
  - Design a multi-layer perceptron for the classification of mobile handsets.
  - Structure of multi-layer perceptron



Biometrics and Digital Forensics

- Optimization for Digital Forensics
  - Output at the first layer of the multi-layer perceptron:

$$\mathbf{y}_i = \mathbf{f}(\mathbf{W}\mathbf{x}_i)$$

  - Objective: minimize the interclass separation and maximize the intraclass separation

$$\min_{\mathbf{W}} J'(\mathbf{W}) \equiv \frac{\sum_{\mathbf{x}_i \in S_0} \left\| \mathbf{f}(\mathbf{W}\mathbf{x}_i) - \frac{1}{N_0} \sum_{\mathbf{x}_i \in S_0} \mathbf{f}(\mathbf{W}\mathbf{x}_i) \right\|^2 + \sum_{\mathbf{x}_j \in S_1} \left\| \mathbf{f}(\mathbf{W}\mathbf{x}_j) - \frac{1}{N_1} \sum_{\mathbf{x}_j \in S_1} \mathbf{f}(\mathbf{W}\mathbf{x}_j) \right\|^2}{\left\| \frac{1}{N_0} \sum_{\mathbf{x}_i \in S_0} \mathbf{f}(\mathbf{W}\mathbf{x}_i) - \frac{1}{N_1} \sum_{\mathbf{x}_j \in S_1} \mathbf{f}(\mathbf{W}\mathbf{x}_j) \right\|^2}$$

Biometrics and Digital Forensics

- Optimization for Digital Forensics
  - Output at the second layer of the multi-layer perceptron:

$$Q\left(\tilde{\mathbf{w}}^T \mathbf{y}_i\right)$$

  - Objective: maximize the separation between two different classes:

$$\max_{\tilde{\mathbf{w}}} \quad \delta$$

subject to $t_i \mathbf{y}_i^T \tilde{\mathbf{w}} \geq \delta$

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Questions and Answers

Thank you!

Let me think…